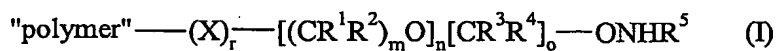


Claims

1. Functionalized polymer of formula I



wherein the symbols have the following meanings

"polymer" soluble linear or branched homopolymers or random copolymers and derivatives thereof selected from the group consisting of alkylene glycol homopolymers, alkylene glycol copolymers, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids and polysaccharides;

$R^1, R^2, R^3,$

R^4, R^5 hydrogen, alkyl, aryl;

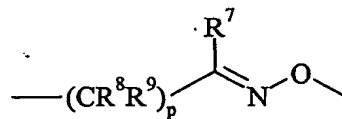
m 2 to 4, wherein the residues R^1 and R^2 may be the same or different in the m groups CR^1R^2 ;

n 0 to 20;

o 0 to 20, wherein in the case of $n = 0$, o is not 0, wherein the residues R^3 and R^4 may be the same or different in the o groups CR^3R^4 ;

r 0 or 1;

X $-(CR^8R^9)_pO-$, $-(CR^8R^9)_pS-$, $-(CR^8R^9)_pNR^6-$, $-(CR^8R^9)_pOC(O)-$, $-(CR^8R^9)_pC(O)O-$, $-(CR^8R^9)_pC(G)N(R^{10})O-$, $-(CR^8R^9)_pN(R^{11})O-$,



wherein one or more groups $-(CR^8R^9)-$ may be replaced by W , whereby a chemically reasonable group is formed;

W $O, NR^{12}, C(G);$

G $S, O, NR^{14};$

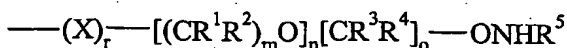
$R^6, R^7, R^8,$

$R^9, R^{10},$

R^{11}, R^{12}, R^{14} hydrogen, alkyl, aryl,

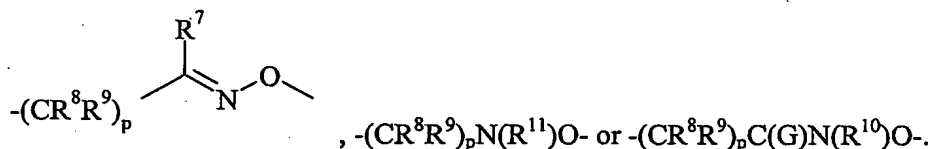
p 0 to 20, wherein the residues R^8 and R^9 may be the same or different in the p groups CR^8R^9 ;

wherein the group



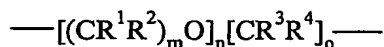
is covalently linked with at least one terminal group or at least one centrally located groups of the "polymer".

2. Functionalized polymer as claimed in claim 1, wherein X is



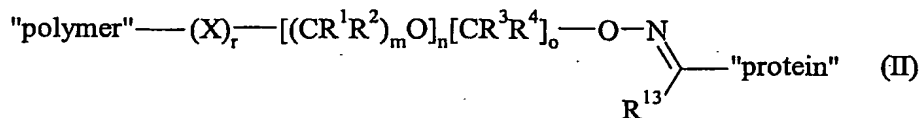
3. Functionalized polymer as claimed in claim 1 or 2, wherein the polymer is hydroxyalkyl starch, dextran or ethylene glycol homopolymer.

4. Functionalized polymer as claimed in any of claims 1 or 3, wherein the group



is $-\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$.

5. Conjugate of formula II



wherein the symbols have the following meanings

"polymer" soluble linear or branched homopolymers or random copolymers and derivatives thereof selected from the group consisting of alkylene glycol homopolymers, alkylene glycol copolymers, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane,

ethylene/maleic anhydride copolymer, polyaminoacids and polysaccharides;

$R^1, R^2, R^3,$

R^4 hydrogen, alkyl, aryl;

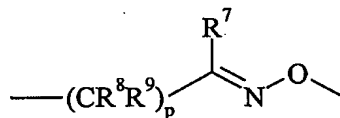
m 2 to 4, wherein the residues R^1 and R^2 may be the same or different in the m groups CR^1R^2 ;

n 0 to 20;

o 0 to 20, wherein in the case of $n = 0$, o is not 0, wherein the residues R^3 and R^4 may be the same or different in the o groups CR^3R^4 ;

r 0 or 1;

X $-(CR^8R^9)_pO-$, $-(CR^8R^9)_pS-$, $-(CR^8R^9)_pNR^6-$, $-(CR^8R^9)_pOC(O)-$, $-(CR^8R^9)_pC(O)O-$, $-(CR^8R^9)_pC(G)N(R^{10})O-$, $-(CR^8R^9)_pN(R^{11})O-$,



wherein one or more groups $-(CR^8R^9)-$ may be replaced by W , whereby a chemically reasonable group is formed;

W $O, NR^{12}, C(G)$;

G S, O, NR^{14} ;

$R^6, R^7, R^8,$

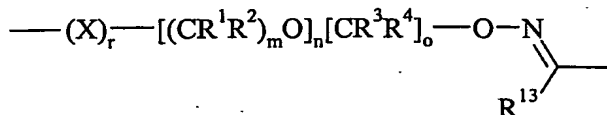
$R^9, R^{10},$

R^{11}, R^{12}, R^{14} hydrogen, alkyl, aryl, preferably hydrogen,

p 0 to 20, wherein the residues R^8 and R^9 may be the same or different in the p groups CR^8R^9 ;

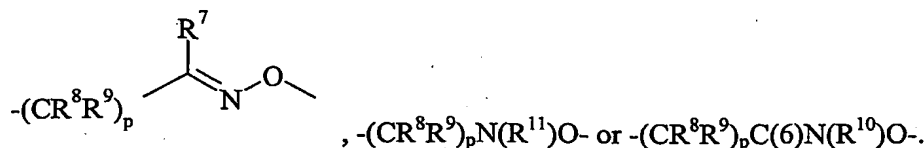
R^{13} hydrogen, alkyl, aryl;

“protein” amino acid sequence prepared by reaction of at least 2 amino acids wherein the group



is covalently linked with at least one terminal group or at least one centrally located group of the “polymer” and the “protein”.

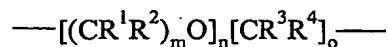
6. Conjugate as claimed in claim 5, wherein X is



7. Conjugate as claimed in claim 5 or 6, wherein the polymer is hydroxyalkyl starch, dextran or ethylene glycol homopolymer.

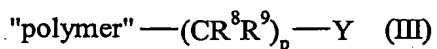
8. Conjugate as claimed in any of claims 5 to 7, wherein the "protein" is selected from the group consisting of EPO, G-CSF, Factor VII, Factor IX, IFN beta, AT III, A1AT, Factor VIII and APC.

9. Conjugate as claimed in any of claims 5 or 8, wherein the group

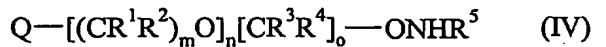


is $-\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$.

10. Process for preparing a functionalized polymer comprising the step of reacting a polymer of formula III



with a compound of formula IV



wherein the symbols have the following meanings

- "polymer" soluble linear or branched homopolymers or random copolymers and derivatives thereof selected from the group consisting of alkylene glycol homopolymers, alkylene glycol copolymers, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids and polysaccharides;

$R^1, R^2, R^3,$

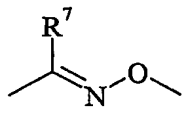
R^4, R^5 hydrogen, alkyl, aryl;

m 2 to 4, wherein the residues R^1 and R^2 may be the same or different in the m groups CR^1R^2 ;

n 0 to 20;

o 0 to 20, wherein in the case of $n = 0$, o is not 0, wherein the residues R^3 and R^4 may be the same or different in the o groups CR^3R^4 ;

Y and Q functional groups, which are suitable to react together to give one of the following linking groups $-O-$, $-S-$, $-NR^6-$, $-OC(O)-$, $-C(O)O-$, $-C(G)N(R^{10})O-$, $-N(R^{11})O-$,



wherein one or more groups $-(CR^8R^9)-$ may be replaced by W , whereby a chemically reasonable group is formed;

W $O, NR^{12}, C(G)$;

G S, O, NR^{14} ;

$R^6, R^7, R^8,$

$R^9, R^{10},$

R^{11}, R^{12}, R^{14} hydrogen, alkyl, aryl;

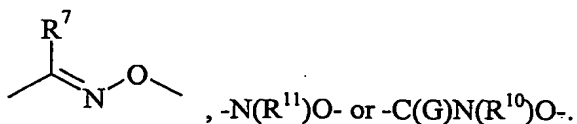
p 0 to 20, wherein the residues R^8 and R^9 may be the same or different in the p groups CR^8R^9 ;

wherein the group

$-(CR^8R^9)_p-Y$

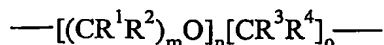
is covalently linked with terminal groups or centrally located groups of the "polymer".

11. Process as claimed in claim 10, wherein Y and Q are functional groups, which are suitable to react together to give the following linking group



12. Process as claimed in claim 10 or 11, wherein the polymer is hydroxyalkyl starch, dextran or ethylene glycol homopolymer.

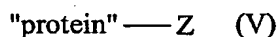
13. Process as claimed in any of claims 10 to 12, wherein the group



is $\text{---CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{---}$.

14. Functionalized polymer as obtainable by a process as claimed in any of claims 10 to 13.

15. Process for preparing a conjugate, comprising the step of reacting a functionalized polymer as claimed in any of claims 1 to 4 or 14 with a functionalized protein of formula V



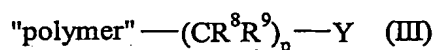
wherein Z is a group comprising a carbonyl group or a group which is suitable of forming a carbonyl group or another group which is reactable with the functionalized polymer, wherein Z is covalently linked with least one terminal group or least one centrally located group of the "protein".

16. Process as claimed in claim 15, wherein a functionalized polymer as claimed in any of claims 2 to 4 is employed.

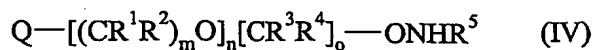
17. Process as claimed in claim 15 or 16, wherein the "protein" is selected from the group consisting of EPO, G-CSF, Factor VII, Factor IX, IFN beta, AT III, A1AT, Factor VIII and APC.

18. Process for preparing a conjugate, comprising the steps

a) reacting a polymer of formula III



with a compound of formula IV



wherein the symbols have the following meanings

“polymer” soluble linear or branched homopolymers or random copolymers and derivatives thereof selected from the group consisting of alkylene glycol homopolymers, alkylene glycol copolymers, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids and polysaccharides;

$R^1, R^2, R^3,$

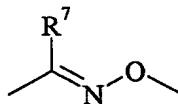
R^4, R^5 hydrogen, alkyl, aryl;

m 2 to 4, wherein the residues R^1 and R^2 may be the same or different in the m groups CR^1R^2 ;

n 0 to 20;

o 0 to 20, wherein in the case of $n = 0$, o is not 0, wherein the residues R^3 and R^4 may be the same or different in the o groups CR^3R^4 ;

Y and Q functional groups, which are suitable to react together to give one of the following linking groups $-O-$, $-S-$, $-NR^6-$, $-OC(O)-$, $-C(O)O-$, $-C(G)N(R^{10})O-$, $-N(R^{11})O-$,



wherein one or more groups $-(CR^8R^9)-$ may be replaced by W , whereby a chemically reasonable group is formed;

W $O, NR^{12}, C(G);$

G $S, O, NR^{14};$

$R^6, R^7, R^8,$

$R^9, R^{10},$

R^{11}, R^{12}, R^{14} hydrogen, alkyl, aryl;

p 0 to 20, wherein the residues R^8 and R^9 may be the same or different in the p groups CR^8R^9 ;

wherein the group

$-(CR^8R^9)_p-Y$

is covalently linked with least one terminal group and/or least one centrally located group of the "polymer", wherein a functionalized polymer is obtained, and

b) reacting the functionalized polymer obtained in step a) with a functionalized protein of formula V

"protein" — Z (V)

wherein Z is a group comprising a carbonyl group or a group which is suitable of forming a carbonyl group or another group which is reactable with the functionalized polymer, wherein Z is covalently linked with least one terminal group and/or least one centrally located group of the "protein".

19. Conjugate as obtainable by a process as claimed in any of claims 15 to 18.

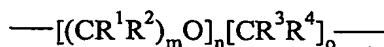
20. A conjugate as claimed in any of claims 5 to 9 or 19 for use in a method for the treatment of the human or animal body.

21. A pharmaceutical composition comprising in a therapeutically effective amount a conjugate as claimed in any of claims 5 to 9 or 19.

22. The pharmaceutical composition as claimed in claim 21, further comprising at least one pharmaceutically acceptable diluent, adjuvant, or carrier.

23. Functionalized polymer as claimed in any of claims 1 to 3, wherein o is from 2 to 20.

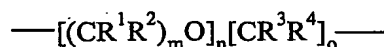
24. Functionalized polymer as claimed in any of claims 1 to 3, wherein the group



is $\text{---CH}_2\text{CH}_2(\text{CH}_3)\text{CH}_2\text{CH}_2\text{---}$.

25. Conjugate as claimed in any of claims 5 to 8, wherein o is from 2 to 20.

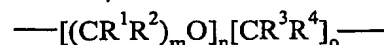
26. Conjugate as claimed in any of claims 5 to 8, wherein the group



is $\text{---CH}_2\text{CH}_2(\text{CH}_3)\text{CH}_2\text{CH}_2\text{---}$.

27. The process as claimed in any of claims 10 to 12, wherein o is from 2 to 20.

28. The process as claimed in any of claims 10 to 12, wherein the group



is $\text{---CH}_2\text{CH}_2(\text{CH}_3)\text{CH}_2\text{CH}_2\text{---}$.

29. Functionalized polymer as obtainable by a process as claimed in claim 27 or 28.

30. The process as claimed in claim 15 or 17, wherein a functionalized polymer as claimed in any of claims 23, 24 or 29 is reacted with the functionalized protein of formula V.

31. The process as claimed in claim 18, wherein o is from 2 to 20.

32. Conjugate obtainable by a process as claimed in claim 30.

33. A conjugate as claimed in any of claims 25, 26 or 32 for use in a method for the treatment of the human or animal body.

34. A pharmaceutical composition comprising in a therapeutically effective amount a conjugate as claimed in any of claims 25, 26 or 32.

35. The pharmaceutical composition as claimed in claim 34, further comprising at least one pharmaceutically acceptable diluent, adjuvant, or carrier.